Author’s response to reviews

Title: Household Fuel Use and Adverse Pregnancy Outcomes in a Ghanaian Cohort Study

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Author’s response to reviews:

Dear editor and referees,

Thank you for your comments and insights on our submission. Following consideration of the comments received, we would like to submit this revised manuscript for further consideration.

Kindly find our point-to-point response to each of the reviewer’s comments below.

We hope with these adjustments and answers to the manuscript will be enough and ready for publication.

On behalf of the co-authors,

Eartha Weber, Kwame Adu-Bonsaffoh, George S Downward and Joyce Browne

#Editorial comments:
Comments from Reviewer 1:

Comment 1: Job well done though the following are my concerns:

There are a number of confounding factors that seem to not have been controlled. It is a known fact that women with little or no education have poor pregnancy/ perinatal outcomes even in settings where "polluting cooking fuel" is not used.

Response:

We adjusted for maternal education as a confounder by incorporating it into the model. See the legends
of Tables 2 and 4 for information on which categories education was divided into and for which confounders were adjusted for (BMI, maternal age, education and socio-economic status by asset index) respectively. The findings remained consistent after adjusting for these factors.

Comment 2: So many things can lead to miscarriage for example the strenuous work involved in collecting firewood.

Response: Unfortunately, specific information on the collection of firewood was not collected. However, the study was undertaken in an urban center where anecdotally most people purchase firewood collected and brought in from the villages.

After reviewing the literature there are no specific studies about the physical labor aspect of collecting firewood on pregnancy outcomes. We have now incorporated one such ongoing study (Kwegyir-Afful et.al. A Liftless Intervention to Prevent Preterm Birth and Low Birthweight Among Pregnant Ghanaian Women: Protocol of a Stepped-Wedge Cluster Randomized Controlled Trial. JMir Res Protoc. 2018). We did however identify literature examining clinical guidelines for heavy lifting and physical exercise although the findings appeared inconclusive and were mainly conducted in higher income countries.

Comment 3: You have not mentioned whether the women were consistent in attending antenatal clinic. Low education is associated with poor antenatal attendance.

Response: Information on regularity of attending antenatal clinic was unavailable. However, the women who participated in this cohort were recruited at <17 weeks gestational age. As this is relatively early in pregnancy for the Ghanaian context (with other studies reporting a median first attendance at 20+ weeks), this is therefore likely to be a group with generally good access to antenatal care.

Comment 4: At what stage (mean) did the women have miscarriages?

Response: Unfortunately, this information was unavailable.

Comment 5: The title could be revised.

Response: After reflection on the title, we have updated it to ‘Household fuel use and adverse pregnancy outcomes in a Ghanaian cohort study’. We think it reflects both the main exposure of interest (household fuel use), main outcomes (pregnancy outcomes), setting (Ghana) and study design (cohort).

Comment 6: The paper needs grammatical corrections.

Response: Prior to resubmission the paper was thoroughly reviewed by a native English speaker.

Comment 7: The discussion is insufficient. You might need to do a more literature search.

It is unclear which aspects of the discussion are considered insufficient. However, we have supplemented the discussion with information from additional sources and have restructured the section to better highlight our findings in the global context. The work by Pope et al. has been heavily referenced as it is a recent and pertinent meta-analysis on the topic, pooling multiple studies together into one summary estimate.
Comments from Reviewer 2:

Comment 1: This is a timely and important study that replicates the Asian data in the African context. This study will inform policy, education and funding priorities. Consider discussing methodology some more. Were there any data on any other potentially confounding variables or co-variables, e.g., nutrition, placentation? PTB, preeclampsia have also been tied to abnormal placentation. (Barjaktarovic M, Korevaar TI, Jaddoe VW, de Rijke YB, Peeters RP, Steegers EA. Human chorionic gonadotropin and the risk of pre-eclampsia: a prospective population-based cohort study. Ultrasound in Obstetrics & Gynecology. 2019 Mar 5. Available at https://obgyn.onlinelibrary.wiley.com/doi/full/10.1002/uog.20256). Style and flow could benefit from some minor help - which shouldn't be too difficult.

Response:

To address the nutrition question, we added a column to the descriptive table which stated whether women used vitamin supplementation in our sample. The vitamin users were equally distributed between both groups. Calorie consumption information was unavailable, but BMI was, which was then adjusted for in the model. We agree that placentation is important, however information on abnormal placentation was unavailable. We did however shortly discuss this as a potential mechanism.

Reviewer #3:
Comment 1: In my opinion, many confounding variables can influence pregnancy outcomes in this study. Therefore, it is recommended:
Many details are not clear in the methodology:

The authors need to provide sufficient details for the reader to be able to understand how give matching criteria and number of exposed and unexposed.

Response:

As this study was a cohort study there were no matching criteria, there was inclusion criteria which is mentioned in Section 2.2 under participants and study size (page 6). The number of exposed and unexposed participants are presented in Table 1(page 9).

Comment 2: Clearly define all outcomes, exposures, predictors, potential confounders and effect modifiers.

Response:

A table of definitions has been included in the supplementary data document.

Comment 3: Describe any efforts to address potential sources of bias.

Response:

Bias was addressed by adjusting for BMI, maternal age, maternal education and SES . Despite this,
residual or unmeasured confounders and other sources of bias may remain. We have included a discussion of this in the manuscript.

Comment 4: Explain how to to the study size as arrived at.
Response:
This study was nested in a cohort study consisting of 1,010 pregnant women, the original purpose of this cohort was to measure those with hypertensive disorders, so the power calculation was based on this (for an expected 100 hypertensive events at least). The flowchart describing the final analyzed sample was derived is included in the supplementary material under Figure S.1. Information regarding study size was embedded in the main texts and tables under the sub-heading ‘participants’:

“Information on main cooking fuel used was available for all 1,010 pregnant Ghanaian women enrolled. Twin pregnancies (n=6), and those with missing outcome data were excluded (n=185), resulting in 819 (82%) women included in the final analysis”

General comments:
The article need to be reviewed by English language editor.

Response:
Prior to resubmission the paper was thoroughly reviewed by a native English speaker.

Comments from Reviewer 4:

Comment 1: This is a well written article that addresses an important topic. The introduction is adequate and addresses what is known about the topic and gaps requiring further studies thus justifying the need for this study. The method is incomplete. Referring readers to other study is enough, there is a need for readers to be able to comprehensively assess a study methodology. Information concerning sampling, recruitment, inclusion and exclusion criteria and study procedure are lacking.

Response:
Additional information regarding recruitment, inclusion, exclusion, and general methodology has been added to the manuscript(page 5-8).

Comment 2: Lastly, there is a need to explain the possible mechanism through which exposure to pollution during cooking could influence perinatal mortality and Apgar score.

Response:
A discussion of possible mechanisms has been added to the discussion (page 14):
“There are several avenues through which the products of solid fuel combustion (e.g. carbon monoxide [CO], particulate matter [PM2.5]) may impact fetal health. Particularly small particles, such as CO may cross the placental barrier where they subsequently act directly upon fetal health and development. For example, CO has a strong affinity for fetal hemoglobin, compromising fetal oxygenation. Further, PM2.5 either acting systemically or via placental deposition, may cause oxidative stress and an inflammatory response, further impacting fetal development. Animal studies have for example, identified that PM2.5 exposure impacts placental morphology and impairs maternal-fetal interaction.”

Comment 3: The broader public health implications and policy implications are not adequately discussed
Response:
A comment regarding implications has been added to the discussion.
“The broader public health implications of cleaner fuel use extend beyond pregnancy and pregnancy outcomes as smoke exposure is linked to a multitude of medical conditions such as respiratory infections, lung cancer, chronic obstructive pulmonary disease, heart disease, and blindness. Furthermore, improvements in air quality have been established to prolong overall life expectancy in the general population”